REMARKS

Claim 4 has been amended to limit the glycoprotein to a glycoprotein that is "resistant to sugar hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide." Support for this amendment can be found in the present specification on page 9, lines 5 to 7, and Test Example 1.

Claim 5 has been canceled.

Claim 7 has been amended to limit the hydrolase cleaving a saccharide of a glycopeptide to "sugar hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide". Additionally, the steps of (a) cleaving a saccharide of a glycopeptide and (b) bonding an aminated complex-type oligosaccharide derivative of the formula (1) to the resulting peptide are recited as being performed at the same time. Support for this amendment can be found in the present specification on page 9, lines 5 to 7, Test Example 1, and Example 3.

The proviso "except for the case where both R2 and R3 are hydrogen or the formula (5), and the case where one of R2 and R3 is a hydrogen atom, with the formula (5) serving as the other thereof", which was deleted when claim 4 was amended in the response filed October 23, 2008, has been reinserted into claims 4 and 7. In claims 4 and 7, the proviso is recited as "except that

R^2 and R^3 are not both hydrogen or the formula (5) at the same time and when one of R^2 and R^3 is hydrogen, the other is not the formula (5)" for clarity. Support for this amendment can be found in the original claims and on page 3, lines 11-13, and page 5, lines 13-15, of the present specification.

No new matter has been added.

Claim Rejections - 35 USC § 103 (a)

Claims 4, 5 and 7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rademacher et al. (D1) in view of Wong et al. (D2). Claims 6 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rademacher et al. (D1) in view of Wong et al. (D2) and further in view of Wright et al. (D3). Each of Rademacher et al. (D1), Wong et al. (D2) and Wright et al. (D3) are specifically identified in the Action. These are the same rejections that were applied to the corresponding claims in the first Office Action dated July 7, 2008.

In the response filed October 23, 2008, to the first Office Action, applicants argued that the glycopeptide of the present application is superior to the asparagine-inked glycopeptide in resistance to sugar hydrolase and exhibits improved stability in blood and prolonged life therein. Furthermore, applicants argued

that the physiologically active molecules are uniform in physiological activity in the glycopeptide of the invention.

However, the Office has maintained the obviousness rejections. Regarding claims 4, 5 and 7, the Office points out that D2 "details that release of the oligosaccharide from the neoglycoprotein was effected by hydrazinolysis rather than simple hydrolysis, providing guidance to one of ordinary skill in the art that hydrolysis of the thiol-linked oligosaccharide would require harsher conditions leading to the degradation of the oligosaccharide." (Action, page 6, lines 5-9 from the bottom of the page). The Office also points out that D2 "teaches this method allows one to obtain glycoproteins with homogeneous carbohydrate structures attached [citation omitted] which provides guidance for one ordinary skill in the art to reasonably expect uniform activity based in the homogeneity of the carbohydrate structures attached to protein." (Action, page 6, lines 1-5 from the bottom of the page).

Regarding claims 6 and 8, the Office points out that antibodies are a subgenus of proteins and similarly a glycosylated antibody is subgenus of glycopeptide.

Applicants respectfully submit that the claims as amended are patentable under 35 U.S.C. § 103(a) over the combinations of D1 and D2 and D1, D2 and D3 for the reasons explained below.

Claims 4 and 6

Claim 4 as amended limits the claimed glycopeptide to one having the specific property that it is "resistant to sugar hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide".

D1 discloses nothing relating to the bonding of a thiol group to an aminated complex-type oligosaccharide derivative.

In D2, the oligosaccharide attached to a peptide is derived from horseradish peroxidase and includes Xyl - and not from a human. On the other hand, the glycopeptide of the present application has a human type oligosaccharide, which does not cause problems such as being an antigen when administered to a human.

Furthermore, regarding the cleavage of an oligosaccharide from a peptide, D2 only shows data on hydrazinolysis of a glycopeptide which involves peptide digestion, but not on hydrolysis of a glycopeptide. There is no data in D2 that shows resistance to sugar hydrolase of the glycopeptide of D2. There are many kinds of hydrolase known in the art, but each hydrolase hydrolyzes a different part of a glycopeptide. The hydrolase used in the present application, "hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide", recognizes the structure of a binding site of a oligosaccharide and a peptide, and the amino

acid sequence around the site, and cleaves the linkage between the oligosaccharide and a peptide, i.e., at the junction between the oligosaccharide and the peptide. D2 does not disclose that the oligosaccharide of D2 is resistant to this kind of hydrolase.

Additionally, the structures of reducing terminals of oligosaccharides are different between the present application and D2: the oligosaccharide of D2 includes Fucose attached to terminal GlcNAc. A hydrolase that recognizes a reducing terminal of oligosaccharide with Fucose does not always recognize a reducing terminal without Fucose. In view of this, a person skilled in the art would not have expected, based on D2, that the glycopeptides of the present application would be resistant to the specified sugar hydrolase as recited in the present claims.

Accordingly, the glycopeptide of amended claim 4 and dependent claim 6 is different from the glycopetide of D2, and has advantageous effects that the glycopeptide has a human type oligosaccharide and is resistant to "hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide." Thus, applicants respectfully submit that a person of ordinary skill in the art would not have prepared the glycopeptide of claim 4 and 6 based on D1 and D2.

Claim 5

Claim 5 has been cancelled. Thus, the rejection regarding to claim 5 has been rendered moot.

Claims 7 and 8

Applicants have amended claim 7 to limit the hydrolase which cleaves a saccharide of a glycopeptide to "sugar hydrolase which cleaves the reducing terminal of an oligosaccharide from a peptide". Furthermore, the steps of (a) cleaving a saccharide of a glycopeptide and (b) bonding an aminated complex-type oligosaccharide derivative of the formula (1) to the resulting peptide are recited in claim 7 as being performed at the same time.

The method of claim 7 relates to a method of (a) cleaving a saccharide of a glycopeptide and (b) bonding an aminated complex-type oligosaccharide derivative of the formula (1) to the resulting peptide. This method allows the protein to maintain its folding while cleaving a non-uniform natural type oligosaccharide and attaching a uniform oligosaccharide to the peptide. This method is provided based on the finding that the aminated complex-type oligosaccharide derivative of the formula (1) of the present application has stronger resistance to hydrolase than Asn-linked oligosaccharide.

D1 discloses nothing relating to the bonding of a thiol group to an aminated complex-type oligosaccharide derivative.

D2 only describes producing a glycopeptide by attaching N-(β-saccharide) haloacetamide to SH-group of cysteine residues of a protein, and that the oligosaccharide is cleaved from the peptide by hydrazinolysis. However, hydrazinolysis, which digests a glycopeptide, is completely different from hydrolysis by the sugar hydrolase of the present invention.

D2 does not confirm whether the glycopeptide of D2 is resistant to hydrolase that cleaves the junction between the oligosaccharide and the peptide. Thus, a person of ordinary skill in the art would not have expected from a reading of D2 that the glycopeptide of the present application is resistant to the hydrolase. Furthermore, D2 does not provide data comparing resistance to the hydrolase of the glycopeptides attached by N-(β-saccharide) haloacetamide-linker to that of an Asn-linked oligosaccharide.

Accordingly, the person of ordinary skill in the art could not have arrived at the method of the present application, that is, the method of (a) cleaving a saccharide of a glycopeptide and (b) bonding a linker-linked oligosaccharide to the resulting peptide on the same peptide by using the distinction of resistance to the hydrolase. Furthermore, considering the suggestion in D2 that Asn residue, which is a binding site of natural Asn-linked

oligosaccharide, has to be substituted with Cys residue, D2 teaches away from the invention of the present application.

Thus, applicants submit that claim 7 and dependent claim 8 are patentable under 35 U.S.C. § 103(a) over D1 and D2.

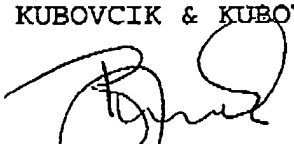
Removal of the 35 U.S.C. § 103(a) rejections and issuance of a Notice of Allowability of the claims are respectfully solicited.

The foregoing is believed to be a complete and proper response to the Office Action dated January 30, 2009.

In the event that this paper is not considered to be timely filed, applicants hereby petition for an appropriate extension of time. The fee for any such extension may be charged to our Deposit Account No. 111833.

In the event any additional fees are required, please also charge our Deposit Account No. 111833.

Respectfully submitted,
KUBOVCIK & KUBOVCIK



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